

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claim 30 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner asserted that the specification, "while being enabling for treatment employing the synergistic combination of polyethylene glycol (PEG) and 4-aminopyridine (4-AP), does not reasonably provide enablement for combination of C₃-C₁₀ polyalkylene glycols and other potassium channel blockers."

This rejection is respectfully traversed. The Examiner is requested to consider claim 30 as amended, which is set forth in Appendix A. Claim 30 was amended in a paper filed February 22, 2002, to recite a method of treating a spinal cord injury, "wherein said polyalkylene glycol is polyethylene glycol" and that the potassium channel blocker is "in the form of 4-aminopyridine." As the Examiner has acknowledged, the specification provides enablement for treatment methods employing the claimed combination of polyethylene glycol and 4-aminopyridine. Reconsideration and withdrawal of the rejection of claims 30 under 35 U.S.C. §112, first paragraph is respectfully requested.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 30 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed

Specifically, the Examiner asserted that the recitation of a method "resulting in a synergistic increase....behavior in said patient" renders the claim indefinite, as to method steps required to achieve the recited results. Applicants respectfully disagree. However, in response to this rejection, Applicants amended claim 30 to recite "contacting said injured spinal cord with a potassium channel blocker . . . so as to produce a synergistic increase in restoration and nerve function of nerve function and reflex behavior in said patient." Thus, the recited synergistic

increase is produced by the contacting of the injured spinal cord with the potassium channel blocker.

Further, the Examiner asserted that "it is not clear what amounts of potassium channel blockers would exhibit synergistic activities with polyethylene glycol." Applicants respectfully disagree. In the method of claim 30, a potassium channel blocker, in the form of 4-aminopyridine, is administered "in an effective amount . . . to produce a synergistic increase in restoration of nerve function and reflex behavior." Thus, the amount of 4-aminopyridine administered is an amount effective to produce a *synergistic* increase in the restoration of nerve function and reflex behavior obtained.

Reconsideration and withdrawal of the rejection of claim 30 under § 112, second paragraph, is respectfully requested.

Rejection under 35 U.S.C. §102(b) Rejection

The Examiner rejected claims 22, 25-29, 38 and 39 are rejected under 35 U.S.C. §102(b) as being anticipated by Davis et al. (Journal of Spinal Disorder, 1990;3(4):299-306). This rejection is respectfully traversed.

Davis et al. describe surgeries for symptomatic unilateral disc protrusion at either L4-5 or L5-S1. The surgeries were accompanied by intraoperative epidural application of methylprednisolone acetate (MP) in a solution containing 28 mg/mL polyethylene glycol (PEG) to increase solubility.

Claim 22 is directed to treatment of a mammalian patient having suffered an injury to its spinal cord, said method comprising contacting the injured spinal cord after the injury but within a period no greater than about 24 hours after said injury with a C₁-C₁₀ polyalkylene glycol in an amount effective to restore nerve impulse conduction through said injured spinal cord.

The Examiner continues to assert that Davis et al. anticipates the claimed method. However the Examiner's argument rests on a faulty conclusion, namely, that disc surgery such as that performed in Davis et al. compresses the spinal cord, thereby causing spinal cord injury. The Examiner attempts to support this conclusion by citing the *Merck Manual of Medical*

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Information - Home Edition, 1997, p. 352, which states that pressure on the spinal cord can come from "a broken vertebra or other bone in the spinal column, a rupture of one or more of the cartilage disks that lie between the vertebrae, an infection (spinal cord abscess), or a tumor in the spinal cord or column" (p. 8 of the Office Action mailed Jan. 28, 2003). In a puzzling twist of logic, the Examiner concludes that "[p]atients undergoing disc excision surgery would be suffered [would suffer?] from compression to their spinal cord *because the bones in the vertebrae column and cartilage disks are removed*" (p. 8, Office Action mailed Jan. 28, 2002, emphasis added) and further that "removing bone from the vertebrae *would cause spinal cord compression*" (pp. 9-10, Office Action mailed Jan. 28, 2003, emphasis added). Applicant asserts that, far from *causing* spinal cord compression, disc excision surgery would, if anything, *relieve* such compression. Conspicuously absent from the *Merck Manual* list of events or agents that cause spinal cord compression is the act of surgery. The *Merck Manual* does not state or even imply that surgery can cause spinal cord compression. To the contrary, the *Merck Manual of Medical Information - Home Edition*, 1997, at p. 353, in describing treatment of spinal cord compression, states that "...the compression must be relieved immediately or the spinal cord may be permanently damaged. *Relief often requires surgery...*" (emphasis added).

The Examiner at pages 9-10 of the Office Action mailed Jan. 28, 2003, also cites Benzel at al., for the proposition that "removal of various bones are necessarily [is necessary?] prior to removing the disk from the vertebrae." However, there is nothing in the record to support the subsequent connection drawn by the Examiner between surgical bone removal and spinal cord compression ("...removing the bone from the vertebrae would cause spinal cord compression," Office Action mailed Jan. 28, 2003, at page 10).

It is respectfully submitted that the Examiner has failed to support, with factual evidence, the assertion that disc excision surgery causes spinal cord compression and thereby spinal cord injury. It is further submitted that the Examiner has provided no reason to doubt the truth or the factual basis of the statements presented by Dr. Scott Shapiro in the Declaration submitted November 15, 2002. In assessing the value of an expert opinion, the Examiner must consider the nature of the matter sought to be established, the strength of any opposing evidence, the interest

in the expert of the outcome of the case, and the presence or absence of factual support for the expert's opinion. MPEP 706.01(c), citing *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985), *cert. denied* 475 U.S. 1017 (1986). Dr. Shapiro is one of the most distinguished and experienced neurosurgeons in the United States and has no interest, as an inventor or otherwise, in the outcome of this case. The nature of the matter to be established (i.e., that disc surgery does not cause spinal cord injury) lends itself to expert testimony because written materials tend not to explicitly state what is commonly assumed by both physicians and patients: that surgeries are not intended to, and typically do not, result in further injury to the patient.

Applicants maintain that the Examiner has not established a *prima facie* case of anticipation (or obviousness, as discussed below). However, even if a *prima facie* case has been established, Applicants point out that the only evidence provided by the Examiner are citations to the *Merck Manual* and *Benzel et al.*, citations that fail to establish a causative connection between disc surgery and spinal cord compression. All of the competent rebuttal evidence taken as a whole should be weighed against the evidence supporting the *prima facie* case. MPEP 716.01(d), citing *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984). The Declaration of Dr. Shapiro, the surgical textbook cited therein, and relevant passages of the Merck manual itself *teach away* from injury of the spinal cord during disc surgery. Dr. Shapiro states that contact with the spinal cord during disc surgery is strictly avoided (Shapiro declaration, para. 8) and that disc surgery, when properly performed, does not result in compression or other contusion of the spinal cord (Shapiro declaration, para. 9). Damage to the spinal cord during disc surgery has been essentially eliminated due to modern surgical techniques (Shapiro declaration, para. 11). The list of complications following thoracic discectomy described in Benzel et al. (Table 27.3, page 248) does not mention any spinal cord related symptoms, nor are any such symptoms discussed in connection with lumbar discectomies (Shapiro declaration, para. 12). The fact that symptoms related to spinal cord injury are not listed implies that they do not occur.

Applicants assert that the a fair evaluation of all the evidence of record compels the conclusion that the disc surgery taught in Davis et al. is not accompanied by spinal cord injury. Reconsideration and withdrawal of the rejection of claims 22, 25-29, 38 and 39 under 35 U.S.C. §102(b) as being anticipated by Davis et al. (Journal of Spinal Disorders, 1990;3(4):299-306), is respectfully requested.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 22, 30-37, 43 and 44 under 35 U.S.C. §103(a) as being unpatentable over Davis et al. (Journal of Spinal Disorders, 1990;3(4):299-306) in view of Potter et al. (Clin Invest Med, 19(4), Suppl.: S80 #533). This rejection is respectfully traversed.

The Examiner is requested to note that claims 31-37 were canceled in the Amendment mailed February 22, 2002, thereby rendering the rejection moot with respect to those claims.

With respect to pending claims 22, 30, 43 and 44, for the reasons stated above, Applicants submit that the primary reference, Davis et al., does not teach disc surgery that compresses the spinal cord, thereby causing spinal cord injury. As Davis et al. does not teach treatment of an injured spinal cord, the Examiner has failed to establish a *prima facie* case of obviousness. Accordingly, it is respectfully submitted that pending claims 22, 30, 43 and 44, directed to treatment of an injured spinal cord, are not rendered obvious over Davis et al. (Journal of Spinal Disorders, 1990;3(4):299-306) in view of Potter et al. (Clin Invest Med, 19(4), Suppl.: S80 #533). Reconsideration and withdrawal of the rejection of claims 22, 30-37, 43 and 44 under 35 U.S.C. §103(a) is respectfully requested.

Allowable Subject Matter

Claims 23-24 were objected to as being dependent upon a rejected base claims. Applicants acknowledge with appreciation the Examiner's statement that the method of treating severed or crushed spinal cord injury, as recited in claims 23 and 24, is not taught or fairly suggested by the prior art.

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Applicants respectfully submit that the base claim, claim 22, is allowable for reasons indicated above. In view thereof, reconsideration and withdrawal of the objection to claims 23 and 24 is respectfully submitted.

Information Disclosure Statement

Applicants submit herewith a Supplemental Information Disclosure Statement, including 1449 form(s) and copies of the documents cited thereon. Consideration of the documents cited on the accompanying 1449 form(s), and return of an initialed copy of the 1449 form(s) indicating consideration of said documents with the next Official Communication, is respectfully requested.

Request for Examiner Interview

Should the Examiner continue to maintain that claims are not yet in condition for allowance, Applicants kindly request a telephone interview with the Examiner and the Supervisory Patent Examiner to discuss any issues that remain outstanding.

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Summary

It is respectfully submitted that the pending claims 22-30, 38-40, 43 and 44 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be in any way assisted or expedited thereby.

Respectfully submitted for
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The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, BOX RCE, Washington, D.C. 20231.

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